What is Evidence-based Medicine?

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"…while the individual man is an insoluble puzzle, in the aggregate, he becomes a mathematical certainty. You can, for example, never foretell what any man will do, but you can say with precision what an average number will be up to. Individuals vary, but percentages remain constant. So says the statistician."

– Sherlock Holmes[1]

In another article in this series, I discussed how randomized controlled trials (RCTs) are the most precise tool we have to determine if a treatment is truly effective and safe (*How Drugs are Evaluated: Patients' Guide to Randomized Clinical Trials*. IFFGD Publication No. 189). Regulatory agencies such as the U.S. Food and Drug Administration (FDA) use data from such trials to approve or reject new drugs. In addition, these data can also assist doctors to determine the best treatment for your functional gastrointestinal (GI) or motility disorder. Trials may also evaluate diets, psychological treatments, complimentary and alternative treatments, even surgical operations, and the value of tests. Data from such trials support *evidence-based medicine* that characterizes modern medicine. Yet, despite its many virtues, scientific medicine is far from perfect. This article explores the advantages, challenges, and way forward for this relatively recent phenomenon.

The Case for Evidence-based Medicine

Randomized trials and evidence-based medicine are late twentieth century innovations. Since the seventeenth century, doctors based their work on sciences such as anatomy and physiology, but often acted upon anecdote, opinion, and tradition. Consequently, they employed many useless and even some harmful treatments – reinforced by the therapeutic benefits of the placebo effect and the passage of time (*What are Placebos: Are They Good for You*? IFFGD Publication No. 172). Doubts about existing treatments and the need to validate new ones led to the development of the randomized controlled trial.

Many illness complaints run their course. All treatments are subject to placebo effects that improve illness (how a person feels), but not disease. Thus, most doctor-patient interactions have a positive outcome even without "effective" treatment. These important positive elements account for the persistence of useless treatments and even famously harmful ones such as bloodletting and purging. Now randomized trials can render such treatments obsolete.

Some treatments are self-evident. Fixation and immobilization of bone fractures and draining abscesses are examples. However, even these may require properly conducted randomized controlled trials to determine the optimum length of immobilization, or the correct antibiotic advice. The validation of most medical treatment requires data from clinical trials.

Challenges to Evidence-Based Medicine

***Cost* –** A pharmaceutical firm will spend enormous amounts for randomized controlled trials required by regulators who judge the effectiveness and safety of a new drug. Few independent researchers can match this, so new drug data comprise a disproportionate share of existing medical evidence. Exuberant marketing of new drugs exaggerates this pharmaceutical bias, while other aspects of medical care struggle for attention. Validating non-regulated aspects of medicine depends upon the initiatives of academic health professionals and is supported insufficiently by government and non-government agencies.

***The Quality of Medical Evidence* –** Although randomized clinical trials are now commonplace, most medical tests and treatments are untested. Many are justified by sound science, and their efficacy is unquestioned. Some rest upon tradition and common sense. Others, such as surgery and psychological treatments, are difficult to evaluate for ethical or practical reasons. Even more difficult to test, are the health effects of diets, lifestyles, and environments – issues important to sufferers of the functional GI disorders. The medical literature

includes a range of reports that contribute to medical evidence, but they vary greatly in quality:

1. *A case report* is a doctor's detailed account of the diagnosis or treatment of a patient's illness. A case report is an anecdote, with little scientific validity. Individual reports are subject to bias, and do not predict that similar patients will behave similarly. (See the Sherlock Holmes "comment" on Page 1.) Case reports are of little value in the functional GI disorders, because individual circumstances among the vast numbers of affected individuals vary so greatly. A report of several similar patients constitutes a *case series*, which expands the experience, but may compound any bias. For rare diseases, such reports may be the only available medical evidence, and provide management ideas to doctors newly confronted with a rare problem. Nevertheless, case reports are the least reliable type of scientific medical reporting.
2. *An observational study* reports patient health outcomes with no intervention. For example, the Framingham study, supported by the U.S. Public Health Service, recruited more than 5,000 adults in 1948. Framingham and other researchers over many years found associations between certain characteristics and heart disease – data that equipped doctors to advise people to exercise, eat less, manage cholesterol, and stop smoking. However, most observational studies are less well conducted or of shorter duration. The association of a disease with a certain diet or lifestyle does not establish causation, since human lives are far too complicated to exclude other factors that may confuse the results. Such studies may suggest a need for further scientific study, but are seldom acceptable at face value. Many such studies reported in the popular press suggest alarming dangers of a certain diet or behavior, only to be contradicted later by another study. Such alarms from uncontrolled observational studies do not serve the public well.
3. *A case-control study* compares a group of people who have a particular condition with others who do not (controls). The controls are an improvement on observational studies, but they are not selected in advance. Therefore, such studies are more subject to bias than a randomized controlled trial.
4. *A cohort study* follows a cohort (group) of people with a certain condition who underwent a certain treatment or other factor. The outcomes for that group are compared with a similar cohort of people without the condition or without the treatment. Lack of blinding, unconcealed allocation, and variations within the groups may bias the results.
5. *A controlled clinical trial* tests a suspected relationship of a treatment, test, or other factor with a good outcome by assigning people to a treatment group or a control group. The gold standard of treatment validation is the *double-blind, randomized, controlled clinical trial*, that controls for bias by randomly allocating participants to either a treatment group, or a control group that receives a placebo, another treatment, or no treatment. Neither the participants nor researchers know whether a subject is on the test treatment or not until the study's end (double-blinding). When properly conducted, such a trial produces the best medical evidence. However, many randomized controlled trials fail because of insufficient numbers, bias, failure of blinding, inappropriate outcome measures, and other pitfalls. In trials or treatments for the functional gastrointestinal disorders, the definition of a good result is especially difficult. Because "improvement" depends upon the opinion of the trial subject, the best outcome measures to employ in randomized trials are controversial. To address this problem, the Rome Foundation sponsored an "Outcomes Conference" in Milwaukee in April of 2009, which was attended by experts from around the world, regulatory authorities, and representatives of the pharmaceutical industry. This commenced a cooperative effort by all parties to determine the best outcome measures for irritable bowel syndrome, dyspepsia, and other functional gut disorders.

***Generalizability* –** The link between data from randomized controlled trials and clinical medicine depends upon their appropriate application to a patient. Subjects selected for a clinical trial should represent a demographically defined population group that has the same disease as the patient. To be eligible to receive a treatment, a patient should fit easily with the test population. However, many factors confound this ideal. Since study subjects are often recruited at university centers or contract research organizations, they may not be typical of patients consulting a family doctor. When only severely affected patients enter a randomized controlled trial, its results may not apply to a less-affected patient. Moreover, among patients no two people are completely alike.

Evidence-based medicine is the "conscientious, explicit and judicious use of the current best evidence from clinical care research in making decisions about the care of individual patients." Thus, physicians must "conscientiously" follow the literature to discover data that might help you. For "judicious use," the physician must judge if you fit the description of the subjects on whom the treatment was successfully tested. Then, after considering your preferences, personal circumstances, cost, and the treatment's side effects, you can decide whether to use it.

The Availability of Medical Evidence – Medical evidence is of little value if it is not readily available where the patient sees his doctor. While specialists can digest data within their own discipline, medical knowledge is so vast and of such variable quality, that it threatens to overwhelm most primary care physicians, to say nothing of patients. In the information age, one might expect that the Internet would help physicians acquire and manage this data. However, medicine has been slow to adopt information technology, and there is so far little systematic attempt to provide reliable and timely medical evidence to physicians.

The Way Forward

Gathering the Data – Testing of all medical treatments and tests is a worthy, if unattainable objective. Many evaluations are unsuccessful because of flawed design or insufficient participants. To overcome this, academics employ various reviewing techniques to collate evidence from several sources. *Review articles* and *consensus conferences* are time-honored methods of assembling and critically analyzing data. However, they lack a structured process and the participants or authors are liable to bias. This is especially true if unpublished data are ignored. Care must also be taken to avoid any influence by an interested party such as a pharmaceutical sponsor.

Systematic reviews and *meta-analyses* attempt more scientific and structured approaches by including all available data and evaluating its quality. Characteristically, criteria for a successful outcome are decided in advance of a systematic review, and several reviewers blindly evaluate the data. Such armchair research is sometimes helpful, but only when high quality data is available – which brings us back to the need for good clinical trials in the first place. Data on the management of the functional GI disorders, while plentiful, are not always of the highest quality. Government, managers, doctors, and patients need more wide-ranging medical evidence, and its acquisition should be a healthcare priority.

Using the Data – The Internet is replete with information of varying trustworthiness. Advertising or testimonials with no foundation of science may beguile doctor and patients alike. Physicians must evaluate the mass of information that comes their way through journals, public media, Internet, industry-sponsored events, and questioning patients. It is technologically possible for all physicians to have information available to them through office computers or hand-held devices. It will prove more difficult to ensure that the information is useful and correct.

For this purpose, members of the *Cochrane Collaboration* evaluate treatments based upon all relevant published and unpublished trial data (www.cochrane.org/reviews/en/). However, maintaining the Cochrane website currently requires the dedication of hundreds of volunteer collaborators. There are national registries, but the ideal would be an international registry where all trials would be promptly available to all. Not only would this help physicians and patients decide treatment, but it would also avoid publication bias and prevent design flaws and duplication.

Conclusions

Evidence-based medicine depends upon the accumulation of data from treating patients. The highest quality evidence is that derived from randomized, placebo-controlled clinical trials. However, such trials are expensive, difficult to execute correctly, and are concentrated upon new drugs. A more comprehensive program aimed at validating all medical acts is a worthy goal, but will require much effort and broad-based funding.

Reference

Doyle AC. The Sign of the Four (Quoting Winwood Reade), pg. 89-158. *The Complete Sherlock Holmes*. New York: Doubleday. 1892.

Further Reading

Thompson WG. *The placebo effect in health: combining science and compassionate care*. New York: Prometheus. 2005.

Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. *Evidence based medicine: what it is and what it isn't*. *BMJ* 1996; 312:71-72.

Goozner M. *The $800 million pill*. Berkeley: University of California Press. 2004.

Thompson WG. *Understanding the irritable gut: the functional gastrointestinal disorders*. McLean: Degnon. 2008.

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